Prioritizing Pediatrics

Accelerating Access to Optimal Pediatric HIV Treatment via a Novel Regulatory Strategy and Public-Private Partnership

CLINTON HEALTH ACCESS INITIATIVE

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A development partnership and innovative regulatory strategy led to the *fastest-ever* approval of a generic HIV medication for children, proving that delays in access to lifesaving commodities do not have to be the status quo.

Introduction

HIV remains a significant public health issue amongst children, with 1.7M children living with HIV (CLHIV) and only 880K on antiretroviral therapy globally in 2021. Over 95% of CLHIV live in low- and middle-income countries, where generic medication is provided through national treatment programs in the public sector.

The Problem

Historically, CLHIV have faced numerous challenges, including sub-optimal formulations and often decades-long development delays, in accessing effective and age-appropriate formulations of HIV medications proven to work in adults. This has resulted in lower levels of viral suppression for children compared to adults, and children bear a disproportionate burden of all AIDS-related deaths relative to the total number of children living with HIV.

Historic Challenges with Pediatric HIV Medication Leading to Sub-Optimal Formulations

Unpalatable

Inconvenient Dosing Frequency

Expensive

Lack of Age-Appropriate Forms

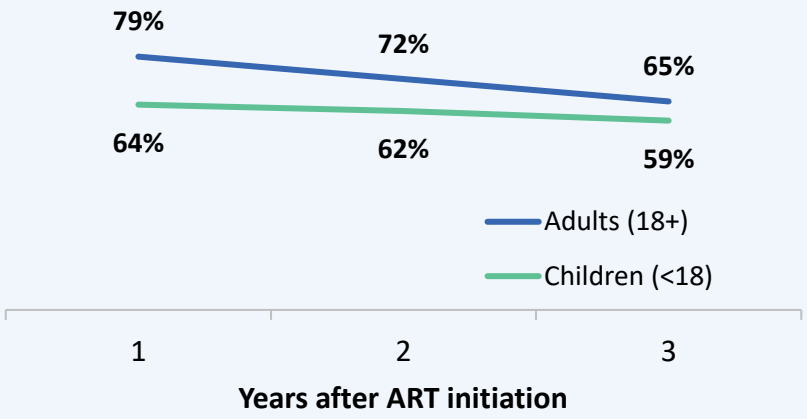
Cold Chain Requirements

Long Development Timelines

These challenges often result in children not having access to optimal HIV medicine, leading to ineffective treatment, intolerable side effects, and poor adherence; resulting in poor clinical outcomes including death.

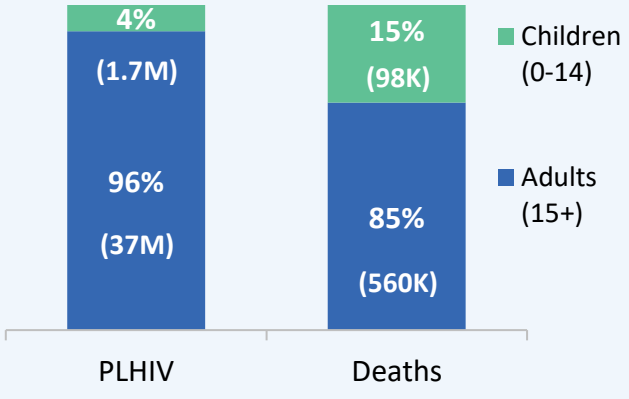
Viral Suppression Rates

PLHIV on ART



PLHIV and AIDS-Related Deaths

2021



Min Han W et al. (2021) Lancet HIV; 8:e766-75

UNAIDS AIDSinfo Database

Dolutegravir (DTG), developed by ViiV Healthcare (ViiV), is the WHO-preferred first- and second-line HIV medication and one of the most widely prescribed antiretrovirals in the world.

Despite being approved by the US Food and Drug Administration (US FDA) for adults in 2013 and being recommended by the World Health Organization as the preferred first- and second-line medication as part of a three-drug regimen for adults and children in 2018, no generic dispersible tablets with approved dosing existed at the time to enable children under 20kg to have access to this medicine—**representing a large gap in access to quality treatment between adults and children.**

Benefits of Pediatric Dolutegravir

- **High Barrier to Resistance**
- **Superior Efficacy**
- **Better Tolerability**
- **Lower Cost & Pill Burden than Other Meds**
- **Easy to Administer**

CHAI, with funding from Unitaid and in partnership with ViiV, implemented a **novel development incentive program** and **innovative regulatory strategy** to dramatically accelerate the development and regulatory approval of a generic pediatric DTG product for use in children under 20kg.

Project Approach

1. Development Incentive Program

Generic manufacturers Mylan (a Viatris company) and Macleods were selected via competitive request for proposal (RfP) as partners to develop DTG 10mg dispersible and scored tablets in parallel with ViiV's development of a 5mg dispersible product.

ViiV conducted clinical trials to demonstrate safety, tolerability, and efficacy of DTG in children >3kg and >4 weeks old.

- Unitaid → Milestone-based financial incentives via CHAI
- ViiV Healthcare → Technical package & ongoing support for formulation and manufacturing process & regulatory support; Clinical supplies
- Clinton Health Access Initiative → Novel regulatory strategy and technical & operational support

→ Viatris, Macleods

Negotiating an *affordable and sustainable* price in advance of product launch (**US $4.50 per 90-count bottle**) was a critical component of the incentive program. This resulted in a 75% price reduction from the existing lopinavir/ritonavir-based standard of care, which could generate **US $60-260 million in savings over five years.**

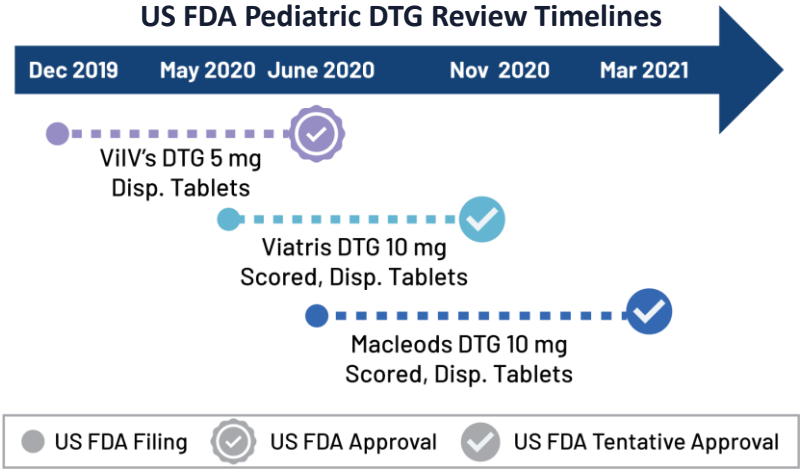
2. Innovative Regulatory Strategy

CHAI, with the support of ViiV, established an innovative regulatory approach enabling *concurrent* US FDA review of the generic products during innovator product review.

This pathway took advantage of the US FDA's PEPFAR review program, and the difference in strengths between the 5mg and 10mg products allowed the generic suppliers to submit their dossiers as 505(b)(2) new drug applications (NDAs) and priority review was obtained.

Advance agreement on this novel pathway with the US FDA improved confidence in filing success.

US FDA Pediatric DTG Review Timelines



At the time of publication, 18 countries have approved DTG 10mg disp. and scored for use, with more registrations pending.

Impact

For the first time ever, a generic HIV medication was filed with the US FDA while the innovator product was still under review. Viatris' generic product received US FDA tentative approval within 5 months of ViiV's product, **the fastest ever regulatory approval of a generic HIV medication** for either adults or children.

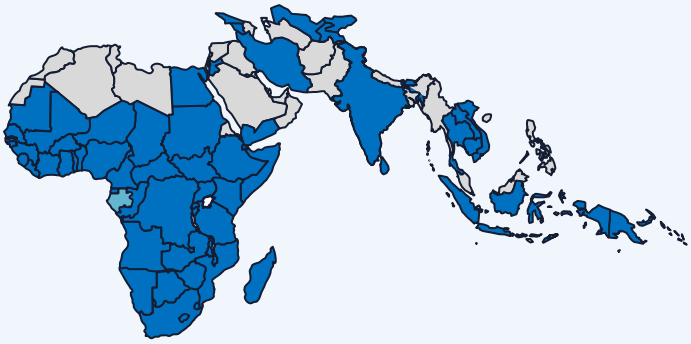
Pediatric DTG Approval Impact Metrics[1]

1) Based on US FDA tentative approval under the PEPFAR program or full US FDA approval where patent protections had expired.

Children in low- and middle-income countries can now receive the same lifesaving medication available in high-income countries without the usual years-long delays. **Generic DTG 10mg dispersible and scored tablets were first dispensed to patients only 11 months after the US FDA approval of the innovator product—a record-breaking timeline that will save lives.**

DTG (10 mg) Disp., Scored Adoption

(as of Q1 2023)



Orders Placed or Delivered*

Procurement Conversation Ongoing**

No data

Not pictured: Belize, Bolivia, Cape Verde, Comoros, Cuba, Ecuador, El Salvador, Haiti, Honduras, Moldova, Nicaragua, Panama, Papua New Guinea, Paraguay, Sao Tome & Principe, Ukraine. Not pictured: Argentina, Bermuda, East Timor*

In just under a year after the first US FDA tentative approval of generic pediatric DTG 10mg disp. scored tablets, **over 25 countries placed orders or had the product delivered,** with over 70 countries at the time of publication**.**

A unified partner position statement supported by GAP-f, proactive normative guidance from WHO, and bold procurement guidance from PEPFAR, all prior to US FDA approval of the innovator product primed the market for rapid introduction.

Further, a catalytic procurement initiative led by CHAI and Unitaid in six countries galvanized broader excitement about the product and accelerated product commercialization immediately after regulatory approval.

Training and other information, education, and communication materials developed by CHAI and civil society organizations helped to further generate demand at the country level.

Lessons Learned

Importance of Innovator Engagement

The active and ongoing support of ViiV, the innovator company, during the generic development process was critical to dramatically reducing development timelines and accelerating patient access.

Collaborative Engagement with US FDA

While unique aspects of the US FDA's PEPFAR review program allowed for this novel regulatory pathway, this has proven that the US FDA is amenable to allowing regulatory discretion that accelerated access.

Photo Credit: Lighthouse Clinic
pDTG adoption data as seen by the APWG and CHAI market intelligence

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